

| | | | | | |
|---|---|----|---|--------------------------|---------------------------|
| Substitute form 1449A/PTO | | | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application Number | To Be Assigned 10/806,523 |
| | | | | Filing Date | Concurrently |
| | | | | First Named Inventor | Nnochiri N. Ekwunibe |
| | | | | Group Art Unit | |
| | | | | Examiner Name | |
| Sheet | 1 | of | 1 | Attorney Docket Number | 9233-64CT |

| U.S. PATENTS AND PATENT PUBLICATIONS | | | | | |
|--------------------------------------|----------|----------------------|-------------------------|--|--|
| Examiner Initials* | Cite No. | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
| | | Number | Kind Code (if known) | | |
| JER | 1 | US-6,506,730 | B1 | Lee et al. | 01/14/2003 |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |
| | | US- | | | |

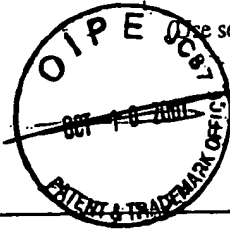
Class/Subclass
514/12

| FOREIGN PATENT DOCUMENTS | | | | | | | |
|--------------------------|-------------|-------------------------|--------|-------------------------|--|--|---|
| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | T |
| | | Office | Number | Kind Code (if known) | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

| | | | |
|--------------------|--------------------|-----------------|---------------|
| Examiner Signature | Jeffrey E. Russell | Date Considered | June 16, 2005 |
|--------------------|--------------------|-----------------|---------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

LIST OF DOCUMENTS CITED BY APPLICANT



(Use several sheets if necessary)

Applicants: Ekwuribe et al.

Filing Date: June 4, 2000

Concurrently

Group

1653

U. S. PATENT DOCUMENTS

| Examiner Initial | Document Number | Date | Name | Class | Subclass | Filing Date if Appropriate |
|------------------|-----------------|----------|------------------|-------|----------|----------------------------|
| JR | 1. 4,179,337 | 12/18/79 | Davis et al. | 435 | 181 | |
| JR | 2. 5,359,030 | 10/25/94 | Ekwuribe | 530 | 303 | |
| JR | 3. 5,405,877 | 04/11/95 | Greenwald et al. | 514 | 772.3 | |
| JR | 4. 5,567,422 | 10/22/96 | Greenwald | 424 | 78.3 | |
| JR | 5. 5,681,811 | 10/28/97 | Ekwuribe | 514 | 8 | |
| | | | | | | |
| | | | | | | |

FOREIGN PATENT DOCUMENTS

| Document Number | Date | Country | Class | Subclass | Translation Yes No |
|-----------------|------|---------|-------|----------|----------------------|
| | | | | | |
| | | | | | |
| | | | | | |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|----|-----|---|
| JR | 6. | Banting et al., "Pancreatic Extracts in the Treatment of Diabetes Mellitus," <i>Can. Med. Assoc. J.</i> , 12: 141-146 (1922). |
| JR | 7. | H. Allcock & F. Lampe, "Contemporary Polymer Chemistry," 394-403 (2nd. ed., 1991). |
| JR | 8. | Y. Chen & G. Baker, "Synthesis and Properties of AMA Amphiphiles," <i>J. Org. Chem.</i> , 64: 6870-6873 (1999). |
| JR | 9. | "Pharmaceutical Research: Official Journal of the American Association of Pharmaceutical Scientists," 3(6): 318-326 (1986). |
| JR | 10. | Coudert et al., "A Novel, Unequivocal Synthesis of Polyethylene Glycols," <i>Synthetic Communications</i> , 16(1): 19-26 (1986). |
| JR | 11. | J. Milton Harris, "Laboratory Synthesis of Polyethylene Glycol Derivatives," <i>J. Macromol. Science - Rev. Macromol. Chem. Phys.</i> , C25(3): 325-373 (1985). |

EXAMINER
EXAMINER

Jeffrey E. Eshel

DATE CONSIDERED

February 11, 2003 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Attorney Docket Number

10/806,523

Serial No.

09/873,777

9233-6401

RECEIVED

To Be

ASSIGNED

LIST OF DOCUMENTS CITED BY APPLICANT

(Use several sheets if necessary)

Applicants:

Ekwuribe et al.

TECH CENTER 1600/2900

Filing Date:

June 4, 2000

Concurrently

Group

1659

1646

U. S. PATENT DOCUMENTS

| Examiner Initial | Document Number | Date | Name | Class | Subclass | Filing Date if Appropriate |
|------------------|-----------------|----------|----------------|-------|----------|----------------------------|
| JR | 1. 5,349,052 | 09/20/94 | Delgado et al. | 530 | 351 | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

FOREIGN PATENT DOCUMENTS

| Document Number | Date | Country | Class | Subclass | Translation Yes No |
|-----------------|----------|---------|-------|----------|----------------------|
| 2. 0 511 903 A2 | 11/04/92 | EPO | C08G | 65/32 | X (Abstract) |
| 3. WO97/14740 | 04/24/97 | PCT | C08G | 65/32 | X |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| | |
|----|---|
| 4. | International Search Report corresponding to PCT/US02/17575; Date of Mailing: September 25, 2002. |
| | |
| | |
| | |
| | |
| | |

EXAMINER
EXAMINER

Jeffrey E. Russell

DATE CONSIDERED

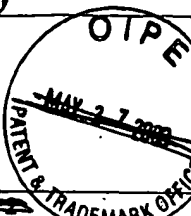
February 11, 2003 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1



Complete if Known

| | |
|------------------------|-------------------|
| Application Number | 09/873,772 |
| Filing Date | June 4, 2001 |
| First Named Inventor | Ekwuribe |
| Group Art Unit | 1654 |
| Examiner Name | Jeffrey E. Russel |
| Attorney Docket Number | 9233.64 CT |

TECH CENTER 1600/2900

U.S. PATENT DOCUMENTS

| Examiner Initials* | Cite No. | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|----------|----------------------|----------------------|---|--|---|
| | | Number | Kind Code (if known) | | | |
| JRL | 1 | 4,223,163 | | Guilloty | 09/16/1980 | 568/618 |
| JRL | 2 | 4,801,575 | | Pardridge | 01/31/1989 | 514/4 |
| JRL | 3 | 5,099,074 | | Mueller et al. | 03/24/1992 | 568/617 |
| JRL | 4 | 5,122,614 | | Zalipsky | 06/16/1992 | 548/520 |
| JRL | 5 | 5,298,410 | | Phillips et al. | 03/29/1994 | 431/188 |
| JRL | 6 | 5,320,840 | | Camble et al. | 06/14/1994 | 401/851 |
| JRL | 7 | 5,714,639 | | Bowman et al. | 02/03/1998 | 568/620 |
| JRL | 8 | 5,428,128 | | Mensi-Fattohi et al. | 06/27/1995 | 530/302 |
| JRL | 9 | 5,468,478 | | Saifer et al. | 11/21/1995 | 424/78,27 |
| JRL | 10 | 5,612,460 | | Zalipsky | 03/18/1997 | 530/311,9 |
| JRL | 11 | 5,637,749 | | Greenwald | 06/10/1997 | 558/6 |
| JRL | 12 | 5,643,575 | | Martinez et al. | 07/01/1997 | 424/194,1 |
| JRL | 13 | 5,854,208 | | Jones et al. | 12/29/1998 | 514/3 |
| JRL | 14 | 6,011,008 | | Domb et al. | 01/04/2000 | 514/8 |

FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T |
|--------------------|----------|-------------------------|--------------------------|----------------------|---|--|---|---|
| | | Office | Number | Kind Code (if known) | | | | |
| JRL | 15 | DE | 196 32 440 A1 | | BASF AG | 02/19/1998 | --- | |
| JRL | 16 | EP | 0 822 218 A2 | | Glenn A. Miller, Michael W. Jorgenson, Richard Budnik | 02/04/1998 | --- | |
| JRL | 17 | JP | 01207320 (Abstract Only) | | Daicel Chem Ind Ltd. | 08/21/1989 | --- | |
| JRL | 18 | PCT | WO 01/12230 | | Myung-Ok Park, Kang Choon Lee | 02/22/2001 | --- | |

OTHER NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T |
|--------------------|----------|--|---|
| JRL | 19 | Francis, G.E., et al., Polyethylene Glycol Modification: Relevance of Improved Methodology to Tumour Targeting, Journal of Drug Targeting, Vol. 3, pp. 321-40 (1996) | |
| JRL | 20 | Guzman, Angel, et al., Effects of Fatty Ethers and Stearic Acid of the Gastrointestinal Absorption of Insulin, PRHSJ, Vol. 9, No. 2, pp. 155-159 (August 1990) | |

| | | | |
|--------------------|-------------------|-----------------|----------------------------|
| Examiner Signature | Jeffrey E. Russel | Date Considered | July 9 2003 / June 16 2005 |
|--------------------|-------------------|-----------------|----------------------------|

10/ 806,523

Institute form 1449A/PTO

Complete if Known

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

~~2~~ ~~1~~ ~~2~~

Application Number

00/873,777 TO BE ASSIGNED

Filing Date

June 4, 2004

First Named Inventor

Ekwuribe

Group Art Unit

1654

Examiner Name

Jeffrey E. Russel

Attorney Docket Number

9233.64C

RECEIVED

FCH CENTER 1600/2900

OTHER NON PATENT LITERATURE DOCUMENTS

| | |
|----|--|
| 21 | Krishnan, B. Radha, et al., <i>Stability and Physical Characteristics of Orally Active Amphiphilic Human Insulin Analog, Methoxy (Polyethylene Glycol) Hexanoyl Human Recombinant Insulin (HIM2)</i> , <i>Proceed. Int'l. Symp. Control. Rel. Bioact. Mater.</i> , Vol. 27 pp. 1038-39 (2000). |
| 22 | Lindsay, D.G., et al., <i>The Acetylation of Insulin</i> , <i>Biochem J.</i> , Vol. 121, pp. 737-745 (1971) |
| 23 | Mesiha, M.S., et al., <i>Hypoglycaemic effect of oral insulin preparations containing Brij 35, 52, 58 or 92 and stearic acid</i> , <i>J. Pharm. Pharmacol.</i> , Vol. 33, pp. 733-34 (1981) |
| 24 | Moghaddam, Amir, <i>Use of polyethylene glycol polymers for bioconjugations and drug development</i> , <i>American Biotechnology Laboratory</i> , pp. 42, 44 (July 2001) |
| 25 | Neubauer, H. Paul, et al., <i>Influence of Polyethylene Glycol Insulin on Lipid Tissues of Experimental Animals</i> , <i>Diabetes</i> , Vol. 32, pp. 953-58 (October 1983) |
| 26 | Shen, Wei-Chiang, et al., (C) Means to Enhance Penetration; (3) Enhancement of polypeptide and protein absorption by macromolecular carriers via endocytosis and transcytosis, <i>Advanced Drug Delivery Reviews</i> , Vol. 8, pp. 93-113 (1992) |
| 27 | Sirokman, Geza, et al., <i>Refolding and proton pumping activity of a polyethylene glycol-bacteriorhodopsin water-soluble conjugate</i> , <i>Protein Science</i> , Vol. 2, pp. 1161-1170 (1993) |
| 28 | Torchilin, Vladimir P., <i>Immunoliposomes and PEGylated Immunoliposomes: Possible Use for Targeted Delivery of Imaging Agents</i> , <i>Immunomethods</i> , Vol. 4, pp. 244-58 (1994) |
| 29 | Wei, Jiang, et al., <i>A Poly(Ethylene Glycol) Water-soluble Conjugate of Porin: Refolding to the Native State</i> , <i>Biochemistry</i> , Vol. 34, pp. 6408-6415 (1995) |
| 30 | Xia, Jiding, et al., <i>Effects of polyoxyethylene chain length distribution on the interfacial properties of polyethylene glycol n-dodecyl ether</i> , <i>Yingyong Huaxue</i> , Vol. 2, No. 4, pp. 59-65 (Abstract Only) (1985) |
| 31 | Zalipsky, Samuel, et al., <i>Peptide Attachment to Extremities of Liposomal Surface Grafted PEG Chains: Preparation of the Long-Circulating Form of Laminin Pentapeptide, YIGSR</i> , <i>Bioconjugate Chem.</i> , Vol. 6, pp. 705-8 (1995) |

Examiner Signature

Jeffrey E. Russel

Date Considered

July 9, 2003 / June 16, 2005

10/806,523

Substitute form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1

Application Number 09/873,797 **C mplet If Known**

Filing Date 06/04/2001 **Concluded**

First Named Inventor Nnochiri N. Ekwuribe

Group Art Unit 1711

Examiner Name Duc Truong

Attorney Docket Number 9233-64CT

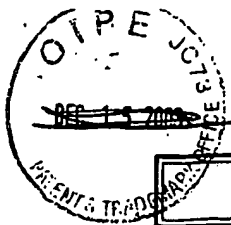
| U.S. PATENTS AND PATENT PUBLICATIONS | | | | | | Class/Subclass |
|--------------------------------------|----------|----------------------|----------------------|---|--|--|
| Examiner Initials* | Cite No. | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear |
| | | Number | Kind Code (if known) | | | |
| JRL | 1 | 2003/0144468 | A1 | Ekwuribe et al. | 07/31/2003 | 5A8 / 425 |
| JRL | 2 | 2003/0087808 | A1 | Soltero et al. | 05/08/2003 | 514 / 3 |
| JRL | 3 | 2003/0083232 | A1 | Soltero et al. | 05/01/2003 | 514 / 3 |
| JRL | 4 | 2003/0089170 | A1 | Soltero et al. | 04/10/2003 | 514 / 2 |
| JRL | 5 | 2003/0050228 | A1 | Ekwuribe et al. | 03/13/2003 | 514 / 3 |
| JRL | 6 | 2003/0027895 | A1 | Ekwuribe et al. | 02/08/2003 | 530 / 399 |
| JRL | 7 | 2003/0027748 | A1 | Ekwuribe et al. | 02/08/2003 | 514 / 3 |
| JRL | 8 | 2003/0004304 | A1 | Ekwuribe et al. | 01/02/2003 | 528 / 425 |
| JRL | 9 | 6,323,311 | B1 | Liu et al. | 11/27/2001 | 530 / 303 |
| JRL | 10 | 6,181,105 | | Ekwuribe et al. | 02/20/2001 | 514 / 3 |
| JRL | 11 | 6,057,292 | | Cunningham et al. | 05/02/2000 | 514 / 12 |
| JRL | 12 | 5,597,797 | | Clark | 01/28/1997 | 514 / 12 |

| FOREIGN PATENT DOCUMENTS | | | | | | | | |
|--------------------------|----------|-------------------------|--------|----------------------|---|--|---|---|
| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T |
| | | Office | Number | Kind Code (if known) | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |

| OTHER NON PATENT LITERATURE DOCUMENTS | | | | T |
|---------------------------------------|----------|--|--|---|
| Examiner Initials* | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | T |
| JRL | 13 | Still et al., <i>Methods of Reducing Hypoglycemic Episodes in the Treatment of Diabetes Mellitus</i> , U.S. Serial No. 10/461,199, filed 06/13/2003 | | |
| JRL | 14 | Radhakrishnan et al., <i>Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same</i> , U.S. Serial No. 10/389,499, filed 03/17/2003 | | |
| JRL | 15 | Soltero et al., <i>Pharmaceutical Compositions of Insulin Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith</i> , U.S. Serial No. 10/382,155, filed 03/05/2003 | | |
| JRL | 16 | Soltero et al., <i>Pharmaceutical Compositions of Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith</i> , U.S. Serial No. 10/382,069, filed 03/05/2003 | | |
| JRL | 17 | Soltero et al., <i>Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same</i> , U.S. Serial No. 10/382,022, filed 03/05/2003 | | |
| JRL | 18 | Ekwuribe et al., <i>Calcitonin Drug-Oligomer Conjugates, and Uses Thereof</i> , U.S. Serial No. 10/166,355, filed 11/08/2002, including Preliminary Amendment dated 02/28/2003 and Supplemental Preliminary Amendment dated 03/31/2003 | | |
| JRL | 19 | Ekwuribe et al., <i>Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same</i> , U.S. Serial No. 09/873,797, filed 06/04/2001 | | |
| JRL | 20 | Ekwuribe et al., <i>Hydrophilic and Lipophilic Balanced Microemulsion Formulations of Free-Form and/or Conjugation-Stabilized Therapeutic Agents Such as Insulin</i> , U.S. Serial No. 09/614,203, filed 07/12/2000 | | |
| JRL | 21 | Hinds et al., <i>Synthesis and Characterization of Poly(ethylene glycol)-Insulin</i> , Bioconjugate Chem., Vol. 11, 2000, pp. 195-201 | | |
| JRL | 22 | Ekwuribe et al., <i>Amphiphilic Prodrugs</i> , U.S. Serial No. 09/474,915, filed 12/31/1999 | | |

Examiner Signature Jeffrey E. Russel Date Considered December 30, 2003 June 16, 2005

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered.



10/806523

~~Applicant~~~~09/873,777~~**ELECTRONIC INFORMATION DISCLOSURE STATEMENT**

Electronic Version v18

Stylesheet Version v18.0

Title of
Invention**MIXTURES OF CALCITONIN DRUG-OLIGOMER
CONJUGATES COMPRISING POLYALKYLENE GLYCOL,
USES THEREOF, AND METHODS OF MAKING SAME**Application Number: ~~09/873777~~ TO BE ASSIGNED

Confirmation Number: 2316

First Named Applicant: Nnochiri Ekwuribe

Attorney Docket Number: 9233.64 CT

Art Unit: 1654

Examiner: Jeffrey E. Russel

Search string: (3256153 or 3868356 or 3919411 or 3950517
or 4003792 or 4044196 or 4087390 or 4093574
or 4100117 or 4229438 or 4253998 or 4277394
or 4338306 or 4348387 or 4410547 or 4469681
or 4554101 or 4579730 or 4585754 or 4662392
or 4684524 or 4698264 or 4717566 or 4774976
or 4772471 or 4797288 or 4839341 or 4840799
or 4849405 or 4917888 or 4935246 or 4946828
or 4957910 or 4963367 or 4963526 or 5013556
or 5055300 or 5055304 or 5089261 or 5093198
or 5157021 or 5162430 or 5164366 or 5202415
or 5206219 or 5286637 or 5283236 or 5292802
or 4472382 or 4994439 or 20020160938 or
20030144468 or 20030087808 or 20030083232
or 20030069170 or 20030050228 or
20030027995 or 20030027748 or
20030004304).pn.

RECEIVED~~DEC 15 2003~~
TECH CENTER 1600/2900**US Patent Documents**

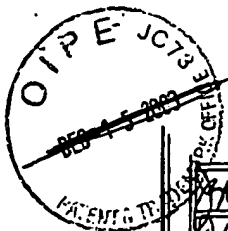
Note: Applicant is not required to submit a paper copy of cited US Patent Documents

| init | Cite.No. | Patent No. | Date | Patentee | Kind | Class | Subclass |
|---------------|----------|------------|------------|----------------|------|-------|----------|
| RL | 1 | 3256153 | 1966-06-14 | Heimlech | | 424 | 497 |
| RL | 2 | 3868356 | 1975-02-25 | Smyth | | 530 | 303 |
| RL | 3 | 3919411 | 1975-11-11 | Glass et al. | | 424 | 78.27 |
| RL | 4 | 3950517 | 1976-04-13 | Lindsay et al. | | 514 | 3 |
| RL | 5 | 4003792 | 1977-01-18 | Mill et al. | | 530 | 303 |

APP_ID=09873777

Jeffrey E. Russel

December 30, 2003 / ~~Page 1 of 2~~
June 16, 2005



10/806,523
~~09/873,777~~

| | | | |
|----|---------|------------------------|------------------------------------|
| 6 | 4044196 | 1977-08-23 | Huper et al. |
| 7 | 4087390 | 1978-05-02 | Shields |
| 8 | 4093574 | 1978-06-06 | Shields |
| 9 | 4100117 | 1978-07-11 | Shields |
| 10 | 4229438 | 1980-10-21 | Fujino et al. |
| 11 | 4253998 | 1981-03-03 | Sarantakis |
| 12 | 4277394 | 1981-07-07 | Fujino et al. |
| 13 | 4338306 | 1982-07-06 | Kitao et al. |
| 14 | 4348387 | 1982-09-07 | Brownlee et al. |
| 15 | 4410547 | 1983-10-13 | Ueno et al. |
| 16 | 4469681 | 1984-09-04 | Brownlee et al. |
| 17 | 4554101 | 1985-11-19 | Hopp |
| 18 | 4579730 | 1986-04-01 | Kidron et al. |
| 19 | 4585754 | 1986-04-29 | Meisner et al. |
| 20 | 4662392 | 1986-05-07 | W. S. 2 Hong et al. |
| 21 | 4684524 | 1987-08-04 | Eckenhoff et al. |
| 22 | 4698264 | 1987-10-06 | Steinke |
| 23 | 4717566 | 1988-01-05 | Eckenhoff et al. |
| 24 | 4774976 | 1988- 02-07 | Sanecke et al. |
| 25 | 4772471 | 1988-09-20 | Vanlerberghe et al. |
| 26 | 4797288 | 1989-01-10 | Sharma et al. |
| 27 | 4839341 | 1989-06-13 | Massey et al. |
| 28 | 4840799 | 1989-06-20 | App. 4859 Massey et al. |
| 29 | 4849405 | 1989-07-18 | Ecanow |
| 30 | 4917888 | 1990-04-17 | Katre et al. |
| 31 | 4935246 | 1990-06-19 | Ahrens |
| 32 | 4946828 | 1990-08-07 | Markussen |
| 33 | 4957910 | 1990-09-18 | Sutton et al. |
| 34 | 4963367 | 1990-10-16 | Ecanow |
| 35 | 4963526 | 1990-10-16 | Ecanow |
| 36 | 5013556 | 1991-05-07 | Woodle et al. |
| 37 | 5055300 | 1991-10-08 | Gupta |
| 38 | 5055304 | 1991-10-08 | Makino et al. |
| 39 | 5089261 | 1992-02-18 | Nitecki et al. |
| 40 | 5093198 | 1992-03-03 | Speaker et al. |
| 41 | 5157021 | 1992-10-02 | Balschmidt et al. |

526/271

525/54.11

525/54.11

525/54.11

514/15

525/54.11

536/330

514/4

514/4

514/557

514/4

514/2

514/3

514/8

137/533.11

424/49

RECEIVED
~~DEC 18 2003~~
TECH CENTER 1600/2900

428/402.2

424/438

137/14

424/450

424/476

514/4

424/493

514/3

424/85.91

424/490

514/3

514/182

424/485

514/3

424/450

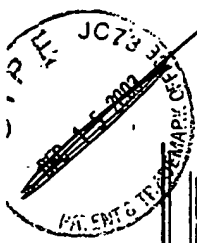
424/409

424/465

424/85.2

428/402.21

514/3



09/873,777
10/806,523

| | | | | |
|-------------------------------------|----|---------|------------|--------------------|
| <input checked="" type="checkbox"/> | 42 | 5162430 | 1992-11-10 | Rhee et al. |
| <input checked="" type="checkbox"/> | 43 | 5164366 | 1992-11-17 | Balschmidt et al. |
| <input checked="" type="checkbox"/> | 44 | 5202415 | 1993-04-13 | Jonassen et al. |
| <input checked="" type="checkbox"/> | 45 | 5206219 | 1993-04-27 | Desai |
| <input checked="" type="checkbox"/> | 46 | 5286637 | 1994-02-15 | Veronese et al. |
| <input checked="" type="checkbox"/> | 47 | 5283236 | 1994-02-01 | Chiou |
| <input checked="" type="checkbox"/> | 48 | 5292802 | 1994-03-08 | Rhee et al. |
| <input checked="" type="checkbox"/> | 49 | 4472382 | 1984-09-18 | Labrie et al. |
| <input checked="" type="checkbox"/> | 50 | 4994439 | 1991-02-19 | Longenecker et al. |

525/54.1
514/3
530/303
514/3
435/183
514/2
525/54.1
514/15
514/3

US Published Applications

Note: Applicant is not required to submit a paper copy of cited US Published Applications

| init | Cite.No. | Pub. No. | Date | Applicant | Kind | Class | Subclass |
|-------------------------------------|----------|-------------|------------|--------------------|-------|-------|----------|
| <input checked="" type="checkbox"/> | 1 | 20020160938 | 2002-10-31 | Brandenburg et al. | | 514 | 3 |
| <input checked="" type="checkbox"/> | 2 | 20030144468 | 2003-07-31 | Ekwuribe et al. | | 528 | 425 |
| <input checked="" type="checkbox"/> | 3 | 20030087808 | 2003-05-08 | Soltero et al. | | 514 | 3 |
| <input checked="" type="checkbox"/> | 4 | 20030083232 | 2003-05-01 | Soltero et al. | | 514 | 3 |
| <input checked="" type="checkbox"/> | 5 | 20030069170 | 2003-04-10 | Soltero et al. | 514/2 | 514 | 3 |
| <input checked="" type="checkbox"/> | 6 | 20030050228 | 2003-03-13 | Ekwuribe et al. | | 514 | 3 |
| <input checked="" type="checkbox"/> | 7 | 20030027995 | 2003-01-02 | Ekwuribe et al. | | 530 | 399 |
| <input checked="" type="checkbox"/> | 8 | 20030027748 | 2003-02-06 | Ekwuribe et al. | | 514 | 3 |
| <input checked="" type="checkbox"/> | 9 | 20030004304 | 2003-01-02 | Ekwuribe et al. | | 528 | 425 |

RECEIVED
DEC 18 2003
TECH CENTER 1600/2900

Signature

| Examiner Name | Date |
|-------------------|-----------------------------------|
| Jeffrey E. Russel | December 30, 2003 / June 16, 2005 |



10/806,523

~~09/873,777~~

ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18

Stylesheet Version v18.0

Title of
InventionMIXTURES OF CALCITONIN DRUG-OLIGOMER
CONJUGATES COMPRISING POLYALKYLENE GLYCOL,
USES THEREOF, AND METHODS OF MAKING SAMEApplication Number: ~~09/073777~~ TO BE ASSIGNED

Confirmation Number: 2316

First Named Applicant: Nnochiri Ekwuribe

Attorney Docket Number: 9233.64CT

Art Unit: 1654

Examiner: Jeffrey E. Russel

Search string: (5304473 or 5308889 or 5312808 or 5324775
or 5328955 or 5405621 or 5413791 or 5415872
or 5438040 or 5444041 or 5446091 or 5457066
or 5461031 or 5504188 or 5506203 or 5518998
or 5523348 or 5529915 or 5545618 or 5550188
or 5597797 or 5606038 or 5631347 or 5646242
or 5650388 or 5658878 or 5681567 or 5693609
or 5693769 or 5700904 or 5707648 or 5738846
or 5747445 or 5747642 or 5750497 or 5763396
or 5766620 or 5824638 or 5830853 or 5830918
or 5843866 or 5849860 or 5853748 or 5856451
or 5866538 or 5866584 or 5874111 or 5898028
or 5902588 or 5905140).pn.

RECEIVED

~~DEC 18 2003~~

TECH CENTER 1600/2906

US Patent Documents

Note: Applicant is not required to submit a paper copy of cited US Patent Documents

| init | Cite.No. | Patent No. | Date | Patentee | Kind | Class | Subclass |
|----------------|----------|------------|------------|-----------------|------|----------|----------|
| 873 | 1 | 5304473 | 1994-04-19 | Belagaje et al. | | 435/69.7 | |
| 873 | 2 | 5308889 | 1994-05-03 | Rhee et al. | | 523/113 | |
| 873 | 3 | 5312808 | 1994-05-17 | Shorr et al. | | 514/6 | |
| 873 | 4 | 5324775 | 1994-06-28 | Rhee et al. | | 525/54.2 | |
| 873 | 5 | 5328955 | 1994-07-12 | Rhee et al. | | 525/54.1 | |
| 873 | 6 | 5405621 | 1995-04-11 | Sipos | | 424/490 | |
| 873 | 7 | 5413791 | 1995-05-09 | Rhee et al. | | 424/422 | |
| 873 | 8 | 5415872 | 1995-05-16 | Sipos | | 424/490 | |

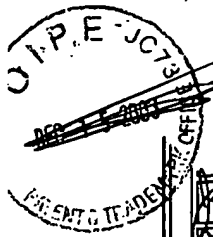
APP_ID=09873777

Jeffrey E. Russel

December 30, 2003

~~Page 1 of 1~~

June 16, 2005



10/806,523.
~~09/873,177~~

| | | | |
|----|---------|------------|-------------------------------|
| 9 | 5438040 | 1995-08-01 | Ekwuribe |
| 10 | 5444041 | 1995-08-22 | Owen et al. |
| 11 | 5446091 | 1995-08-29 | Rhee et al. |
| 12 | 5457066 | 1995-10-10 | Frank et al. |
| 13 | 5461031 | 1995-10-24 | De Felippis |
| 14 | 5504188 | 1996-04-02 | Baker et al. |
| 15 | 5506203 | 1996-04-09 | Backstrom et al. |
| 16 | 5518998 | 1996-05-21 | Backstrom et al. |
| 17 | 5523348 | 1996-06-04 | Rhee et al. |
| 18 | 5529915 | 1996-06-25 | Phillips et al. |
| 19 | 5545618 | 1996-08-13 | Buckley et al. |
| 20 | 5550188 | 1996-08-27 | Rhee et al. |
| 21 | 5597797 | 1997-01-28 | Clark et al. |
| 22 | 5606038 | 1997-02-25 | Regen |
| 23 | 5631347 | 1997-05-20 | Baker et al. |
| 24 | 5646242 | 1997-07-08 | Baker et al. |
| 25 | 5650388 | 1997-07-22 | Shorr et al. |
| 26 | 5658878 | 1997-08-19 | Backstrom et al. |
| 27 | 5681567 | 1997-10-28 | Baker et al. |
| 28 | 5693609 | 1997-12-02 | Baker et al. |
| 29 | 5693769 | 1997-12-02 | Kahne et al. |
| 30 | 5700904 | 1997-12-23 | Baker et al. |
| 31 | 5707648 | 1998-01-13 | Yiv |
| 32 | 5738846 | 1998-04-14 | Greenwald et al. |
| 33 | 5747445 | 1998-05-05 | Backstrom et al. |
| 34 | 5747642 | 1998-05-05 | De Felippis |
| 35 | 5750497 | 1998-05-12 | Havelund et al. |
| 36 | 5763396 | 1998-06-09 | Weiner et al. |
| 37 | 5766620 | 1998-06-16 | Heiber et al. |
| 38 | 5824638 | 1998-10-20 | Burnside et al. |
| 39 | 5830853 | 1998-11-03 | Backstrom et al. |
| 40 | 5830918 | 1998-11-03 | Sportsman et al. |
| 41 | 5843866 | 1998-12-01 | Park Weiner et al. |
| 42 | 5849860 | 1998-12-15 | Hakimi et al. |
| 43 | 5853748 | 1998-12-29 | New |
| 44 | 5856451 | 1999-01-05 | Olsen et al. |

514/3

514/2

525/54.1

435/68.1

514/4

530/304

514/4

514/3

525/54.1

435/188

514/12

525/54.1

514/12

536/6.5

530/303

RECEIVED

530/303

514/6

~~DEC 10 2003~~

514/3

424/18.1

TECH CENTER 1600/2900

514/3

536/5

530/305

424/450

424/85.7

514/4

530/304

514/3

514/3

424/436

514/3

514/4

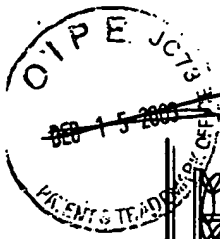
514/648

504/116

528/370

424/439

530/402



10/806523
~~09/17/03~~ 177

| | | | | |
|---------------|----|---------|------------|------------------|
| PP | 45 | 5866538 | 1999-02-02 | Norup et al. |
| XL | 46 | 5866584 | 1999-02-02 | Cincotta et al. |
| PP | 47 | 5874111 | 1999-02-23 | Maitra et al. |
| PP | 48 | 5898028 | 1999-04-27 | Jensen et al. |
| PP | 49 | 5902588 | 1999-05-11 | Greenwald et al. |
| PP | 50 | 5905140 | 1999-05-18 | Hansen |

514/3
514/288
724/799
514/4
724/278.1
530/303

Signature

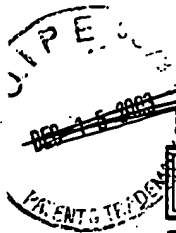
| Examiner Name | Date |
|-------------------|-------------------|
| Jeffrey G. Russel | December 30, 2003 |

June 16, 2005

RECEIVED

~~DEC 18 2003~~

TECH CENTER 1600/2900



10/806.523

09/873,777

ELECTRONIC INFORMATION DISCLOSURE STATEMENT

Electronic Version v18

Stylesheet Version v18.0

Title of
InventionMIXTURES OF CALCITONIN DRUG-OLIGOMER
CONJUGATES COMPRISING POLYALKYLENE GLYCOL,
USES THEREOF, AND METHODS OF MAKING SAMEApplication Number: ~~09/873,777~~ TO BE ASSIGNED

Confirmation Number: 2316

First Named Applicant: Nnochiri Ekwuribe

Attorney Docket Number: 9233.64

Art Unit: 1654

Examiner: Jeffrey E. Russel

Search string: (5907030 or 5922675 or 5932462 or 5942248
or 5948751 or 5952008 or 5952297 or 5962267
or 5968549 or 5969040 or 5981709 or 5985263
or 6004574 or 6025325 or 6034054 or 6042822
or 6043214 or 6051551 or 6057292 or 6063761
or 6093391 or 6113906 or 6165976 or 6177087
or 6191105 or 6200602 or 6211144 or 6248363
or 6251856 or 6258377 or 6268335 or 6306440
or 6309633 or 6310038 or 6323311 or 6335316
or 6342225).pn.

RECEIVED

~~DEC 15 2003~~
TECH CENTER 1600/2900

US Patent Documents

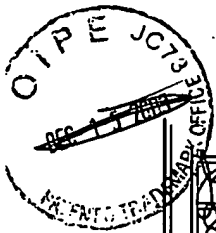
Note: Applicant is not required to submit a paper copy of cited US Patent Documents

| init | Cite.No. | Patent No. | Date | Patentee | Kind | Class | Subclass |
|------------|----------|------------|------------|--------------------|------|----------|----------|
| <i>JER</i> | 1 | 5907030 | 1999-05-25 | Shen et al. | | 530/331 | |
| <i>JER</i> | 2 | 5922675 | 1999-07-13 | Baker et al. | | 514/4 | |
| <i>JER</i> | 3 | 5932462 | 1999-08-03 | Harris et al. | | 435/188 | |
| <i>JER</i> | 4 | 5942248 | 1999-08-24 | Barnwell | | 424/457 | |
| <i>JER</i> | 5 | 5948751 | 1999-09-07 | Kimer et al. | | 514/4 | |
| <i>JER</i> | 6 | 5952008 | 1999-09-14 | Backstrom et al. | | 424/499 | |
| <i>JER</i> | 7 | 5952297 | 1999-09-14 | De Felippis et al. | | 514/3 | |
| <i>JER</i> | 8 | 5962267 | 1999-10-05 | Shin et al. | | 435/69.4 | |
| <i>JER</i> | 9 | 5968549 | 1999-10-19 | New et al. | | 424/450 | |
| <i>JER</i> | 10 | 5969040 | 1999-10-19 | Hallahan et al. | | 525/54.1 | |

APP_ID=09873777

Jeffrey E. Russel

December 30, 2003 / ~~Page 1 of 2~~
June 16, 2005



10/806.523

~~09/873.777~~

| | | | |
|----|---------|------------|--------------------|
| 11 | 5981709 | 1999-11-09 | Greenwald et al. |
| 12 | 5985263 | 1999-11-16 | Lee et al. |
| 13 | 6004574 | 1999-12-21 | Backstrom et al. |
| 14 | 6025325 | 2000-02-15 | Campfield et al. |
| 15 | 6034054 | 2000-03-07 | De Felippis et al. |
| 16 | 6042822 | 2000-03-28 | Gilbert et al. |
| 17 | 6043214 | 2000-03-28 | Jensen et al. |
| 18 | 6051551 | 2000-04-18 | Hughes et al. |
| 19 | 6057292 | 2000-05-02 | Cunningham et al. |
| 20 | 6063761 | 2000-05-16 | Jones et al. |
| 21 | 6093391 | 2000-07-25 | Kabanov et al. |
| 22 | 6113906 | 2000-09-05 | Greenwald et al. |
| 23 | 6165976 | 2000-12-26 | Backstrom et al. |
| 24 | 6177087 | 2001-01-23 | Greenwald et al. |
| 25 | 6191105 | 2001-02-20 | Ekwuribe et al. |
| 26 | 6200602 | 2001-03-13 | Watts et al. |
| 27 | 6211144 | 2001-04-03 | Havelund |
| 28 | 6248363 | 2001-06-19 | Patel et al. |
| 29 | 6251856 | 2001-06-26 | Markussen et al. |
| 30 | 6258377 | 2001-07-10 | New et al. |
| 31 | 6268335 | 2001-07-31 | Brader |
| 32 | 6306440 | 2001-10-23 | Backstrom et al. |
| 33 | 6309633 | 2001-10-30 | Ekwuribe et al. |
| 34 | 6310038 | 2001-10-30 | Havelund |
| 35 | 6323311 | 2001-11-27 | Liu et al. |
| 36 | 6335316 | 2002-01-01 | Hughes et al. |
| 37 | 6342225 | 2002-01-29 | Jones et al. |

530/351

424/85.2

424/434

514/2

514/4

424/85.7

514/3

514/3

514/12

514/3

424/85.1

424/174.1

514/3

424/278.1

514/3

424/463

514/4

424/497

514/3

424/450

514/3

424/499

424/85.1

514/4

530/303

514/3

424/193.1

RECEIVED

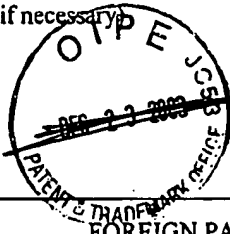
DEC 18 2004
TECH CENTER 1600/2300

Signature

| Examiner Name | Date |
|-------------------|-----------------------------------|
| Jeffrey E. Russel | December 30, 2003 / June 16, 2005 |

10/806,543
Applicants (ny)
~~Sh...~~

| | | |
|--|---|---|
| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) | Attorney Docket Number 9233-64CT | RECEIVED DEC 8 1 1993 TECH CENTER 1600/2900 |
| | Applicants: Ekwuribe et al. | |
| | Filing Date June 4, 2001 CONCURRENTLY | Group 1654 |



FOREIGN PATENT DOCUMENTS

| | | Document Number | Date | Country | Class | Subclass | Translation Yes No |
|----|-----|-----------------|----------|---------------|-------|----------|----------------------|
| BR | 1. | GB 1 492 997 | 11/23/77 | Great Britain | _____ | _____ | |
| BR | 2. | EP 0 031 567 | 07/08/81 | EPO | _____ | _____ | |
| BR | 3. | JP 1 254 699 | 10/11/89 | Japan | _____ | _____ | |
| BR | 4. | 0483465B1 | 05/06/92 | EPO | _____ | _____ | |
| BR | 5. | WO93/01802 | 02/04/93 | PCT | _____ | _____ | |
| BR | 6. | WO95/09831 | 04/13/95 | PCT | _____ | _____ | |
| BR | 7. | EP 0 483 465 | 08/02/95 | EP | _____ | _____ | |
| BR | 8. | WO95/30641 | 11/16/95 | PCT | _____ | _____ | |
| BR | 9. | EP 0 597 007 | 10/16/96 | EP | _____ | _____ | |
| BR | 10. | EP 0 621 777 | 11/09/96 | EP | _____ | _____ | |
| BR | 11. | EP0797615B1 | 01/10/97 | EPO | _____ | _____ | |
| BR | 12. | WO98/07745 | 02/26/98 | PCT | _____ | _____ | |
| BR | 13. | WO99/32134 | 07/01/99 | PCT | _____ | _____ | |
| BR | 14. | WO99/65941 | 12/23/99 | PCT | _____ | _____ | |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|----|-----|--|
| BR | 15. | Abuchowski, A. and F. F. Davis "Soluble Polymer-Enzyme Adducts" pp. 367-383, <i>Enzymes as Drugs</i> , Ed. J. S. Holcenberg, John Wiley (1981) |
| BR | 16. | Agarwal et al. "Polymethacrylate-based Microparticulates of Insulin for Oral Delivery: Preparation and In Vitro Dissolution Stability in the Presence of Enzyme Inhibitors" <i>International Journal of Pharmaceutics</i> 225:31-39 (2001) |
| BR | 17. | Akiyama et al. "The Synthesis of New Derivatives of 1-β-D-Arabinofuranosylcytosine" <i>Chem. Pharm. Bull.</i> 26(3):981-984 (1978) |
| BR | 18. | Allaudeen et al. "Orally Active Insulin: A Single Insulin Conjugate Selected for Future Studies" 60th Annual Meeting of the American Diabetes Assoc., Atlanta, GA, June 2000 (Abstract) |
| BR | 19. | Anderson et al. "HIM2, a Novel Modified Insulin, has Improved Systemic Pharmacokinetics in Normal Dogs, Compared to Unmodified Insulin" American Diabetes Association 62nd Annual Meeting, June 2002 (Abstract) |
| BR | 20. | Ansell et al. "Application of Oligo-(14-amino-3,6,9,12-tetraoxatetradecanoic acid) Lipid Conjugates as Steric Barrier Molecules in Liposomal Formulations" <i>Bioconjugate Chem.</i> 10:653-666 (1999) |

EXAMINER
*EXAMINER

Jeffrey C. Russell


DATE CONSIDERED

January 7, 2004 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

10/806523

~~Sheet 2 of 2~~

| | | | |
|---|--|--|--|
| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office | | Attorney Docket Number 9233-64CT | Serial No. 891873,777 TO BE ASSIGNED |
| LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) | | Applicants: Ekwuribe et al. | |
|  | | Filing Date June 4, 2001 CONCURRENTLY | Group 1654 |
| 21 | Aoshima et al. "N ⁴ -Behenoyl-1-β-D-Arabinofuranosylcytosine as a Potential New Antitumor Agent" <i>Cancer Research</i> 37:2481-2486 (1977) | | |
| 22 | Baker, D. C. et al. "Prodrugs of 9-β-D-Arabinofuranosyladenine. 1. Synthesis and Evaluation of Some (Acyl) Derivatives" <i>J. Med. Chem.</i> 21(12):1218-1221 (1978) | | |
| 23 | Banting et al. "Pancreatic Extracts in the Treatment of Diabetes Mellitus: Preliminary Report" <i>Can. Med. Assoc. J.</i> 145(10):1281-1286 (1991) | | |
| 24 | Baudys et al. "Stabilization and Intestinal Absorption of Human Calcitonin" <i>J. Contr. Rel.</i> 39:141-144 (1996) | | |
| 25 | Baudys et al. "Synthesis and Characterization of Different Glycosylated Derivatives of Insulin" <i>Proced. Intern. Symp. Cont. Rel. Bioactive. Mater.</i> 19:210-211 (1992) | | |
| 26 | Block, Lawrence H. "Pharmaceutical Emulsions and Microemulsions" <i>Pharmaceutical Dosage Forms: Disperse Systems</i> Vol. 2, Ed. Lieberman et al., pp.47-109 (1996) | | |
| 27 | Boccu et al. "Pharmacokinetic Properties of Polyethylene Glycol Derivatized Superoxide Dismutase" <i>Pharm. Res. Comm.</i> 14:113-120 (1982) | | |
| 28 | Bone et al. "Successful Treatment of an Insulin Dependent Rat Model of Human Type I Diabetes with Orally Active Insulin" Program and Abstracts, 4th International Workshop on Lessons from Animal Diabetes, Omiya, Japan, November 1994 (Abstract) | | |
| 29 | Bone et al. "Successful Treatment of Type I Diabetes with Orally-Active Insulin: Studies in The Insulin Dependent BB/S Rat" Program and Abstracts, 55th Annual Meeting of the American Diabetes Association, Atlanta Georgia, June 1995 (Abstract) | | |
| 30 | Brange and Volund "Insulin Analogs with Improved Pharmacokinetic Profiles" <i>Advanced Drug Delivery Reviews</i> 35:307-335 (1999) | | |
| 31 | Brange et al. "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations" <i>Pharm. Res.</i> 9(6):715-726 (1992) | | |
| 32 | Brange et al. "Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation Product During Storage of Pharmaceutical Preparations" <i>Pharm. Res.</i> 9(6):727-734 (1992) | | |
| 33 | Brange, J. "Galenics of Insulin: The Physico-Chemical and Pharmaceutical Aspects of Insulin and Insulin Preparations" Novo Research Institute, Denmark, pp. 18-100 (1987) | | |
| 34 | Chien, Y. W., Novel Drug Delivery Systems, pp. 678-679, Marcell Deffer, Inc., New York, N.Y. (1992) | | |
| 35 | Cleland et al. "Emerging Protein Delivery Methods" <i>Current Opinion in Biotechnology</i> 12:212-219 (2001) | | |
| 36 | Clement et al. "Effects of Multiple Doses of Orally Administered Hexyl Insulin M2 (HIM2) on Postprandial Blood Glucose (PPG) Concentrations in Type 1 Diabetic (T1) Patients" American Diabetes Association 62nd Annual Meeting, June 2002 (Poster) | | |
| 37 | Clement et al. "Oral Insulin Product Hexyl-Insulin Monoconjugate 2 (HIM2) in Type 1 Diabetes Mellitus: The Glucose Stabilization Effects of HIM2" <i>Diabetes Technology & Therapeutics</i> 4(4):459-466 (2002) | | |
| 38 | Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract) | | |
| 39 | Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Poster) | | |

 EXAMINER
 *EXAMINER

Jeffrey E. Muse

DATE CONSIDERED

January 7, 2004 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

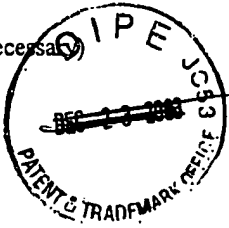
June 16, 2005

6/806,523

Sheet 3 of 3

| | | | |
|--|--|--|---|
| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office | | Attorney Docket Number 9233-64CT | Serial No. 09/873,797 TO BE ASSIGNED |
| LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) | | Applicants: Ekwuribe et al. | |
| | | Filing Date June 4, 2001 | Group 654 |

| | |
|----|--|
| 40 | Conradi et al. "The Influence of Peptide Structure on Transport Across Caco-2 Cells" <i>Pharm. Res.</i> 8(12):1453-1459 (1991) |
| 41 | Coombes et al. "Biodegradable Polymeric Microparticles for Drug Delivery and Vaccine Formulation: the Surface Attachment of Hydrophilic Species Using the Concept of Poly(Ethylene Glycol) Anchoring Segments" <i>Biomaterials</i> 18:1153-1161 (1997) |
| 42 | Damge et al. "Poly(alkyl cyanoacrylate) Nanospheres for Oral Administration of Insulin" <i>Journal of Pharmaceutical Sciences</i> 86(12):1403-1409 (Dec. 1997) |
| 43 | Dandona et al. "Effect of an Oral Modified Insulin on Blood Glucose Levels in Fasting and Fed Type 1 Diabetic Patients Receiving a 'Basal' Regimen of Injected Insulin" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract) |
| 44 | Delgado et al. "The Uses and Properties of PEG-Linked Proteins" <i>Critical Reviews in Therapeutic Drug Carrier Systems</i> 9(3,4):249-304 (1992) |
| 45 | Ekwuribe et al. <i>Calcitonin Drug-Oligomer Conjugates, and Uses Thereof</i> , U.S. Serial No. 10/166,355, filed 11/08/2002, including Preliminary Amendment dated 02/26/2003 and Supplemental Preliminary Amendment dated 03/31/2003 |
| 46 | Ekwuribe et al. <i>Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same</i> , U.S. Serial No. 09/873,797, filed 06/04/2001 |
| 47 | Ekwuribe, Nnochiri "Conjugation-Stabilized Polypeptide Compositions, Therapeutic Delivery and Diagnostic Formulations Comprising Same, and Method of Making and Using the Same" <i>Biotechnology Advances</i> 14(4):575-576 (1996) (Abstract) |
| 48 | Engel et al. "Insulin: Intestinal Absorption as Water-in-Oil-in-Water Emulsions" <i>Nature</i> 219:856-857 (1968) |
| 49 | Fasano, Alessio "Innovative strategies for the oral delivery of drugs and peptides" <i>TIBTECH</i> 16:152-157 (1998) |
| 50 | Forst et al. "New Aspects on Biological Activity of C-peptide in IDDM Patients" <i>Exp. Clin. Endocrinol. Diabetes</i> 106:270-276 (1998) |
| 51 | Gish et al. "Nucleic Acids. 11. Synthesis of 5'-Esters of 1-β-D-Arabinofuranosylcytosine Possessing Antileukemic and Immunosuppressive Activity" <i>J. Med. Chem.</i> 14(12):1159-1162 (1971) |
| 52 | Gombotz & Pettit "Biodegradable Polymers for Protein and Peptide Drug Delivery" <i>Bioconjugate Chem.</i> 6:332-351 (1995) |
| 53 | Hashimoto et al. "Synthesis of Palmitoyl Derivatives of Insulin and Their Biological Activities" <i>Pharmaceutical Research</i> 6(2):171-176 (1989) |
| 54 | Hinds et al. "Synthesis and Characterization of Poly(ethylene glycol)-Insulin Conjugates" <i>Bioconjugate Chem.</i> 11:195-201 (2000) |
| 55 | Hong et al. "Nucleoside Conjugates. 7. Synthesis and Antitumor Activity of 1-β-D-Arabinofuranosylcytosine Conjugates of Ether Lipids" <i>J. Med. Chem.</i> 29:2038-2044 (1986) |
| 56 | Hostetler et al. "Synthesis and Antiretroviral Activity of Phospholipid Analogs of Azidothymidine and Other Antiviral Nucleosides" <i>The Journal of Biological Chemistry</i> 265(11):6112-6117 (1990) |
| 57 | Igarashi et al. "Biologically Active Peptides Conjugated with Lecithin for DDS" <i>Proceed. Intern. Symp. Cont. Rel. Bioactiv. Mater.</i> 17:367-368 (1990) |
| 58 | Kemmner et al. "On the Nature and Subcellular Localization of the Proinsulin Converting Enzymes" <i>Federation Proceedings</i> 30(Abstract 924):1210Abs (1971) |




RECEIVED
TECH CENTER 1600/2900
JUN 16 2005

EXAMINER
*EXAMINER

Jeffrey E. Russell

DATE CONSIDERED January 8, 2004 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| | | | |
|---|-----|--|--|
| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office | | Attorney Docket Number 9233-64 CT | Serial No. 09/873,777 TO BE ASSIGNED |
| LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) | | | |
|  | | Applicants: Ekwuribe et al. | |
| | | Filing Date June 4, 2001 CONCURRENTLY | Group 1654 |
| 59 | JRN | Kemmler et al. "Studies on the Conversion of Proinsulin to Insulin: I. Conversion in Vitro with Trypsin and Carboxypeptidase B" <i>The Journal of Biological Chemistry</i> 246(22):6786-6791 (1971) | |
| 60 | JRN | King et al. "Preparation of Protein Conjugates with Alkoxypolyethylene Glycols" <i>Int. J. Peptide Protein Res.</i> 16:147-155 (1980) | |
| 61 | JRN | Kipnes et al. "Control of Postprandial Plasma Glucose by an Oral Insulin Product (HIM2) in Patients with Type 2 Diabetes" <i>Emerging Treatments and Technologies</i> 26:2 (2003) | |
| 62 | JRN | Kipnes et al. "The Effects of an Oral Modified Insulin on Postprandial Blood Glucose Levels in Patients with Type 2 Diabetes Mellitus" <i>American Diabetes Association Annual Meeting (June 2001) (Poster)</i> | |
| 63 | JRN | Kipnes et al. "The Effects of an Oral Modified Insulin on Postprandial Blood Glucose Levels in Patients with Type 2 Diabetes" <i>American Diabetes Association Annual Meeting (June 24, 2001) (Abstract)</i> | |
| 64 | JRN | Kube, D.M. "Multitalented Proteins Play a Key Role in Therapeutics" <i>Genomics and Proteomics</i> (Sept. 2002) | |
| 65 | JRN | Maislos et al. "The Source of the Circulating Aggregate of Insulin in Type I Diabetic Patients is Therapeutic Insulin" <i>J. Clin. Invest.</i> 77:717-723 (1986) | |
| 66 | JRN | Savva & Huang "Effect of PEG Homopolymer and Grafted Amphiphilic PEG-Palmityl on the Thermotropic Phase Behavior of 1,2-Dipalmitoyl-SN-Glycero-3-Phosphocholine Bilayer" <i>Journal of Liposome Research</i> 9(3):357-365 (1999) | |
| 67 | JRN | Marschutz et al. "Oral Peptide Drug Delivery: Polymer-Inhibitor Conjugates Protecting Insulin from Enzymatic Degradation In Vitro" <i>Biomaterials</i> 21:1499-1507 (2000) | |
| 68 | JRN | Musabayane et al. "Orally Administered, Insulin-Loaded Amidated Pectin Hydrogel Beads Sustain Plasma Concentrations of Insulin in Streptozotocin-Diabetic Rats" <i>Journal of Endocrinology</i> 164:1-6 (2000) | |
| 69 | JRN | Nucci et al. "The Therapeutic Value of Poly(ethylene Glycol)-Modified Proteins" <i>Ad. Drug. Del. Rev.</i> 6:133-151 (1991) | |
| 70 | JRN | Oka et al. "Enhanced Intestinal Absorption of a Hydrophobic Polymer-Conjugated Protein Drug, Smancs, in an Oily Formulation" <i>Pharm. Res.</i> 7(8):852-855 (1990) | |
| 71 | JRN | Pang, David C. "Bridging Gaps in Drug Discovery and Development" <i>Pharmaceutical Technology</i> 22:82-94 (Nov. 1998) | |
| 72 | JRN | Patel et al. "Oral Administration of Insulin By Encapsulation Within Liposomes" <i>FEBS Lett.</i> 62(1):60-63 (1976) | |
| 73 | JRN | Price, JC <i>Polyethylene Glycol</i> , pp. 355-361 (not dated) | |
| 74 | JRN | Puskas et al. "Investigation of Chymotrypsin Digestion Profile of Orally Active Insulin Conjugate HIM2" <i>AAPS Pharm. Sci.</i> 3(3) 2001 (Abstract) | |
| 75 | JRN | Radhakrishnan et al. "Chemical Modification of Insulin with Amphiphilic Polymers Improves Intestinal Delivery," <i>Proceed. Intl. Symp. Control. Rel. Bioact. Mater.</i> 25:124-125 (1998) (Abstract) | |
| 76 | JRN | Radhakrishnan et al. "Oral Delivery of Insulin: Single Selective Modification at B29-LYS With Amphiphilic Oligomer" Program and Abstracts, 1999 National Meeting of the Amer. Assoc. Pharm. Scient., New Orleans, LA (1999) (Abstract) | |
| 77 | JRN | Radhakrishnan et al. "Structure-Activity Relationship of Insulin Modified with Amphiphilic Polymers" Program and Abstracts, 1998 National Meeting of the Amer. Assoc. Pharm. Scient., San Francisco, CA <i>Pharm. Sci.</i> 1(1):S-59 (1998) (Abstract) | |
| 78 | JRN | Radhakrishnan et al. <i>Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same</i> , U.S. Serial No. 10/389,499, filed 03/17/2003 | |

EXAMINER
*EXAMINER


Jeffrey E. Russell

DATE CONSIDERED January 8, 2004 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

10/806 533

~~10/806 533~~

| | | | |
|---|--|---|--|
| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office | | Attorney Docket Number 9233-64CT | Serial No. 09/873,777 TO BE ASSIGNED |
| LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) | | Applicants: Ekwuribe et al. | |
|  | | Filing Date June 4, 2001 CONCURRENTLY | Group 1654 |
| 79 | Ratner, R. E. et al. "Persistent Cutaneous Insulin Allergy Resulting from High-Molecular Weight Insulin Aggregates" <i>Diabetes</i> 39:728-733 (1990) | | |
| 80 | Richards et al. "Self-Association Properties of Monomeric Insulin Analogs Under Formulation Conditions" <i>Pharmaceutical Research</i> 15(9):1434-1441 (1998) | | |
| 81 | Robbins et al. "Antibodies to Covalent Aggregates of Insulin in Blood of Insulin-Using Diabetic Patients" <i>Diabetes</i> 36:838-841 (1987) | | |
| 82 | Russell-Jones, G. J. "Vitamin B12 Drug Delivery" <i>Proceed. Intern. Symp. Control. Rel. Bioactive. Mater.</i> 19:102-103 (1992) | | |
| 83 | Saffran et al. "A Model for the Study of the Oral Administration of Peptide Hormones" <i>Can. J. Biochem. Sci.</i> 57:548-553 (1979) | | |
| 84 | Saffran, M. et al. "A New Approach to the Oral Administration of Insulin and Other Peptide Drugs" <i>Science</i> 233:1081-1084 (1986) | | |
| 85 | Santiago et al. "Oral Immunization of Rats with Influenza Virus M Protein (M1) Microspheres" <i>Proceed. Intern. Symp. Cont. Rel. Bioactive. Mater.</i> 19:116-117 (1992) | | |
| 86 | Shah and Shen "Transcellular Delivery of an Insulin-Transferrin Conjugate in Enterocyte-like Caco-2 Cells" <i>Journal of Pharmaceutical Sciences</i> 85(12):1306-1311 (1996) | | |
| 87 | Shichiri et al. "Enteral Absorption of Water-in-Oil-in-Water Insulin Emulsions in Rabbits" <i>Diabetologia</i> 10:317-321 (1974) | | |
| 88 | Soltero et al. <i>Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same</i> U.S. Serial No. 10/382,022, filed 03/05/2003 | | |
| 89 | Soltero et al. <i>Pharmaceutical Compositions of Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith</i> U.S. Serial No. 10/382,069, filed 03/05/2003 | | |
| 90 | Soltero et al. <i>Pharmaceutical Compositions of Insulin Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith</i> U.S. Serial No. 10/382,155, filed 03/05/2003 | | |
| 91 | Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" <i>Clinical Pharmacol. Therap.</i> 69(2):P95 (Feb. 2001) (Abstract) | | |
| 92 | Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Slide Presentation Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001 | | |
| 93 | Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001 (Handout) | | |
| 94 | Still et al. "Magnitude and Variability of Pharmacokinetic and Glucodynamic Responses to Modified Human Insulin Administered Orally to Healthy Volunteers" <i>Diabetes Research and Clinical Practice</i> 56:S77 (2002) | | |
| 95 | Still et al. <i>Methods of Reducing Hypoglycemic Episodes in the Treatment of Diabetes Mellitus</i> , U.S. Serial No. 10/461,199, filed 06/13/2003 | | |
| 96 | Still, J. Gordon "Development of Oral Insulin: Progress and Current Status" <i>Diabetes/Metabolism Research and Reviews</i> 18(1):S29-S37 (2002) | | |
| 97 | Still, J. Gordon "Oral Insulin Development" Slide Presentation, VI International St. Barts Symposium Diabetes 2000: Therapy and Technology, London, England, May 12, 2000 | | |
| 98 | Szeleifer et al. "Spontaneous Liposome Formation Induced by Grafted Poly(Ethylene Oxide) Layers: Theoretical Prediction and Experimental Verification" <i>Proceedings of the National Academy of Sciences of the United States of America</i> 95(3):1032-1037 (1998) | | |

EXAMINER

*EXAMINER.

Jeffrey E. Russel

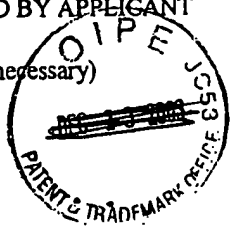
DATE CONSIDERED

January 8, 2004 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

10/806,523

~~Shaw 1-1-86~~

| | | | |
|--|--|--|--|
| FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) | | Attorney Docket Number 9233-64CT | Serial No. 09/033,977 TO BE ASSIGNED |
|  | | Applicants: Ekwuribe et al. | |
| | | Filing Date June 4, 2001 CONCURRENTLY | Group 1654 |
| 99. | Taniguchi et al. "Synthesis of Acyloyl Lysozyme and Improvement of its Lymphatic Transport Following Small Intestinal Administration in Rats" <i>Proceed. Intern. Symp. Control. Rel. Bioactiv. Mater.</i> 19:104-105 (1992) | | |
| 100. | Uchio et al. "Site-Specific Insulin Conjugates with Enhanced Stability and Extended Action Profile" <i>Advanced Drug Delivery Reviews</i> 35:289-306 (1999) | | |
| 101. | Vreeland et al. "Molar Mass Profiling of Synthetic Polymers by Free-Solution Capillary Electrophoresis of DNA-Polymer Conjugates" <i>Analytical Chemistry</i> 73(8):1795-1803 (2001) | | |
| 102. | Wahren et al. "Role of C-peptide in Human Physiology" <i>Am. J. Physiol. Endocrinol. Metab.</i> 278:E759-E768 (2000) | | |
| 103. | Zalipsky et al. "Attachment of Drugs to Polyethylene Glycols" <i>Eur. Polym. J.</i> 19(12):1177-1183 (1983) | | |
| 104. | Ziv and Bendayan "Intestinal Absorption of Peptides Through the Enterocytes" <i>Microscopy Research and Technique</i> 49:346-352 (2000) | | |

RECEIVED
~~DEC 3 2003~~
TECH CENTER 1600/2900

EXAMINER
 *EXAMINER

Jeffrey E. Russel

DATE CONSIDERED

January 8, 2004 / June 16, 2005

Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

| | | | | | |
|-------|---|----|---|------------------------|-----------------|
| Sheet | 1 | of | 1 | Attorney Docket Number | 014811-242.64CT |
|-------|---|----|---|------------------------|-----------------|

NON PATENT LITERATURE DOCUMENTS

[illegible]

| | | | |
|-----------------------|--------------------|--------------------|---------------|
| Examiner Signature | Jeffrey E. Russell | Date Considered | June 16, 2005 |
|-----------------------|--------------------|--------------------|---------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S.

Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☒ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.